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HOMEOSTATIC MECHANISMS FOR THE COMPENSATION OF CUTANEOUS SULFUR LOSSES*

DAPHNE A. ROE, M.D., M.R.C.P.

It has been repeatedly observed that psoriatic patients will maintain an adequate nutritional status even in the presence of chronic generalized exfoliation (1). Indeed, it has been demonstrated that exfoliation of 17 gm. of scale per square meter of body surface per day is necessary before negative nitrogen balance occurs (2). Even at this level of cutaneous loss, clinical evidence of protein malnutrition has not been observed unless such complicating factors as serum loss are present or corticosteroids are administered. These observations have suggested that homeostatic mechanisms exist for the compensation of these nutrient losses from the skin. This hypothesis does not rest primarily on any theory of the kinetics of the psoriatic process (3), but rather on the general physiological concept of the maintenance of the *milieu interieur*. It was considered desirable to investigate the problem of homeostatis utilizing sulfur balance techniques since sulfur losses from the integument can be correlated directly with scale loss (4). Studies have therefore been conducted to compare the sulfur losses in a group of psoriatic patients with those in a control group of subjects.

PATIENTS AND METHODS

The investigations were carried out in the metabolic ward of the Clinical Nutrition Unit at Cornell University. Six control subjects were chosen for study and eight psoriatic patients. The dietary intake of the subjects in both the control and patient groups was adjusted so that a relatively constant body weight was maintained throughout the study period except in one control subject, an obese girl in whom a deliberate weight loss was induced. The subjects were instructed in the techniques for metabolic collection of excreta, including the wearing of garments designed for the collection of scale and sweat (5). Following this period of instruction and dietary adjustment the subjects were studied through sequential six-day metabolic periods varying in total length from twelve to seventy-two days. A brilliant blue fecal dye (6) marker was given at the beginning of each metabolic period to facilitate the separation of stool collections. Scale and sweat collections were each of 48 hours duration. Scale collections were removed from the collection garments into tared bags and sweat collections were made by extraction of the garments as previously described (5). Precautions were taken to avoid contamination of excreta with extraneous sulfur containing materials. Dietary aliquots as well as urine, fecal, scale and sweat samples were analyzed with respect to the sulfur content and the urinary partition of sulfur was determined. Estimations of sulfur were carried out utilizing atomic absorption spectrometry for the estimation of barium and thus indirectly of sulfate-sulfur in the excreta and other biological materials (7). Organic sulfur was oxidized to the inorganic form prior to each analysis (8, 9).

RESULTS

In the control group, it was observed that the absorption of sulfur, i.e., the intake minus the fecal output was correlated with the urinary inorganic sulfate excretion. This relationship held over a range of intake varying from 2 to 5 grams of sulfur per six-day metabolic period and was found to exist whether the subjects were in positive or negative sulfur balance during the study period. Divergence from this direct relationship was found in the psoriatic group. In these subjects the urinary inorganic sulfate excretion was lower than that predicted by the regression line of sulfate excretion on sulfur absorption for the control subjects (Fig. I).

Differences were found between the urinary partition of sulfur in the patient and control groups. In the control group, the percentage of total sulfur excreted as inorganic and total sulfate sulfur was significantly higher than in the patient group (Table I). The percentage urinary excretion of sulfate increased as the sulfur absorption in the control group ($r = 0.99$) but correlation was not found between these parameters in the patient group. In the

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* From the Clinical Nutrition Unit, Graduate School of Nutrition, Cornell University, Ithaca, New York.

control group the mean sulfur absorption was 0.599 gm per 24 hours (Range 0.330–0.881 gm per 24 hours), and in the patient group the mean sulfur absorption per 24 hours was 0.479 gm (Range 0.250–0.745).

Whether patients or controls were in negative or positive sulfur balance depended on intake as well as on absorption (intake-fecal loss). There was no evidence that positive or negative sulfur balance was characteristic of the psoriatic as against the control group, though two patients with generalized exfoliative psoriasis showed positive sulfur balance (Tables II and III).

When the psoriatic scale losses in grams per six-day metabolic period were plotted against the inorganic sulfate excretion per gram of sulfur absorbed, over the same period, it was shown that the urinary inorganic sulfate excretion diminished with increasing scale loss (Fig. 2). The total sulfur content of scale samples in the patient group showed a constant level. The mean and standard devia-

TABLE I

Urinary partition of sulfur in patient and control groups

(Values expressed as percentages of the total urinary sulfur losses)

	Inorganic sulfate sulfur	Ester sulfate sulfur	Total sulfate sulfur	Neutral sulfur
Patients				
Mean	57	11	68	32
Range	(28–71)	(5–33)	(55–87)	(13–45)
Controls				
Mean	73	7	80	20
Range	(56–88)	(1–13)	(64–92)	(8–36)

TABLE II

Sulfur Intake, Average Excretions and Balance (gm./day)

(Psoriatic Group)

Patient	Sex	Age	Intake	Urinary loss	Fecal Loss	Cutaneous loss	Sulfur balance per day	No. met. period
F.K.	F	42	0.457	0.555	0.103	0.006	−.207	2
			0.490	0.525	0.089	0.007	−.131	2
T.R.	M	55	0.467	0.428	0.071	0.004	−.036	2
			0.498	0.441	0.087	0.003	−.033	2
J.K.	M	36	0.649	0.548	0.179	0.029	−.107	2
			0.599	0.460	0.145	0.022	−.028	2
P.B.	M	52	0.794	0.577	0.049	0.214	−.046	1
S.C.	M	36	0.703	0.435	0.213	0.043	+.012	1
			0.810	0.460	0.199	0.045	+.106	1
			0.724	0.430	0.196	0.555	+.043	1
M.F.	M	56	0.494	0.403	0.244	0.037	−.190	1
			0.542	0.362	0.255	0.037	−.112	1
S.B.	M	21	0.788	0.672	0.136	0.003	−.023	1
			0.822	0.807	0.121	0.003	−.109	1
P.B.	F	31	0.620	0.297	0.070	0.034	+.219	1
			0.577	0.340	0.122	0.096	+.019	1
			0.577	0.338	0.146	0.077	+.016	1
			0.577	0.251	0.128	0.081	+.117	1
			0.577	0.185	0.128	0.049	+.215	1
			0.577	0.170	0.148	0.050	+.209	1
			0.663	0.156	0.110	0.070	+.327	1

TABLE III

Sulfur Intake, Average Excretions and Balance (gm/day)
(Control Group)

Patient	Sex	Age	Intake	Urinary Loss	Fecal loss	Cutaneous Loss	Sulfur Balance Per Day	No. Metab. Period
F.P.	M	49	0.554	0.465	0.095	0.006	−.012	2
R.W.	F	18	0.604	0.770	0.080	0.002	−.248	2
			0.543	0.693	0.129	0.002	−.281	3
			0.453	0.571	0.123	0.002	−.243	3
M.A.	F	60	0.739	0.753	0.093	-	−.107	4
L.D.	M	57	0.852	0.782	0.172	-	−.102	1
			0.957	0.770	0.135	-	+.052	2
M.S.	F	80	0.894	0.872	0.013	0.001	+.008	1
			0.728	0.753	0.011	0.001	−.037	3
			0.772	0.772	0.012	0.001	−.013	3
W.M.	M	44	0.600	0.623	0.118	-	−.141	2
			0.631	0.696	0.140	-	−.205	3

* A hyphen (-) denotes that complete cutaneous sulfur losses were not obtained.

tion for the sulfur content of exfoliated scale as expressed in mgm per gram of defatted scale was 7.86 ± 0.15. Thus, it has been found that the sulfur losses from exfoliated scale vary directly with the weight of scale lost.* Graphic correlation has been obtained showing the relationship between the total cutaneous sulfur losses and the urinary inorganic sulfate loss per gram of sulfur absorbed per six-day metabolic period (Fig. 3). Correction of the cutaneous sulfur losses for total body surface area did not, in the present group of subjects, cause significant change in this relationship (Fig. 4). In case P.B. (female),† a case of extensive psoriasis, which was followed by generalized exfoliation during the period of study, there was a delayed compensation for increased cutaneous sulfur losses (Table IV).

It was not considered feasible to separate the cutaneous losses of scale from those in the sweat, since contamination of sweat with scale particles was inevitable with the technique employed. The area of the body surface was calculated using the height and weight relationships of Sendroy and Cecchini (10).

The cutaneous losses of sulfur in the control group were extremely small, ranging from 30.6 to 39.6 mgm per six-day metabolic period (Table II). It can therefore be seen that the cutaneous sulfur losses in the normal subjects did not substantially alter the overall sulfur balance.

DISCUSSION

The results of these investigations show that cutaneous losses of sulfur incurred through exfoliation of scale are compensated by diminished urinary excretion of inorganic sulfate. Thus, provided that intake of sulfur is adequate and fecal losses are not excessive, sulfur balance may be maintained. The data accumulated does not indicate whether with chronic cutaneous losses of great magnitude, this compensatory mechanism may reach a limit so that sulfur losses from the integument might thereafter induce a sulfur deficit. However, this might be anticipated on the assump-

* The mean and standard deviation for the sulfur content of defatted stratum corneum obtained from the legs of control subjects expressed in mgm per gram was 8.29 ± 0.19.

† In case P.B., a female with exfoliative psoriasis, supplementary L-methionine was administered daily during the final six-day metabolic period to give 86 mgm per day of sulfur from this source. The excretion of urinary inorganic sulfate was not increased (Table IV). This single observation indicates that in a subject with massive cutaneous losses, oxidation of methionine may be markedly decreased.

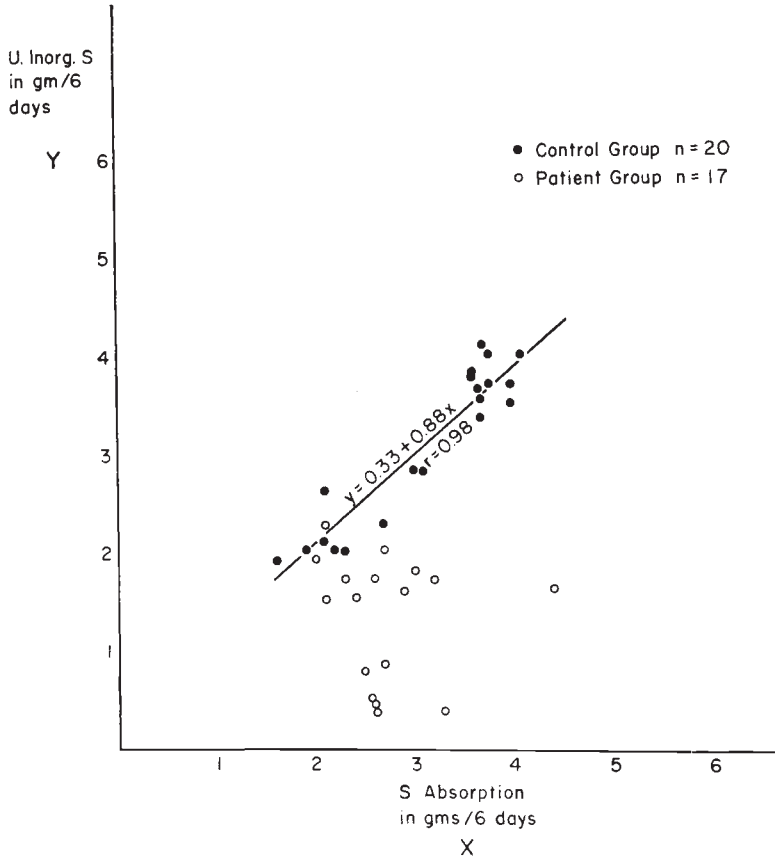

FIG. 1. Correlation of urinary sulfate values with sulfur absorption in control group and divergence of values in psoriatic group.

tion that inorganic sulfate excretion may reach a certain minimal level.

It has been pointed out by Becker, et al. (11) that the plasma inorganic sulfate level is determined by a number of variables such as protein catabolism, absorption from the gastrointestinal tract, and glomerular-tubular balance. These authors showed that in normal subjects, the reabsorption of inorganic sulfate is limited by a maximal rate ($Tmso_4$), but is not dependent on the glomerular filtration rate. The tubular transfer rate was found to vary markedly from person to person. In dogs, it has been demonstrated that administration of a synthetic low protein diet causes an increase in plasma sulfate concentration and it has been suggested that this is due to increased tubular reabsorption (12). Since the levels of plasma inorganic sulfate were not measured in subjects included in the present study, it is not possible to define whether the observed decreases in sulfate excretion with increased cutaneous losses of sulfur were due to decreased protein catabolism or to increased tubular reabsorption or whether both of these factors were operative.

The early studies of Cathcart and Green demonstrated that most of the sulfur excreted as urinary inorganic sulfate in man results from the catabolism of ingested protein rather than displacement of protein from tissues. However, in starvation, urinary sulfur was shown to be derived from endogenous sources (13). It was shown by Wilson that the sulfur moiety of the proteins is mobilized prior to nitrogen, both in the storage and breakdown of protein (14). Urinary inorganic sulfate normally constitutes 60–90% of the total sulfur in the urine (15). It is the largest and the most variable fraction, because as mentioned

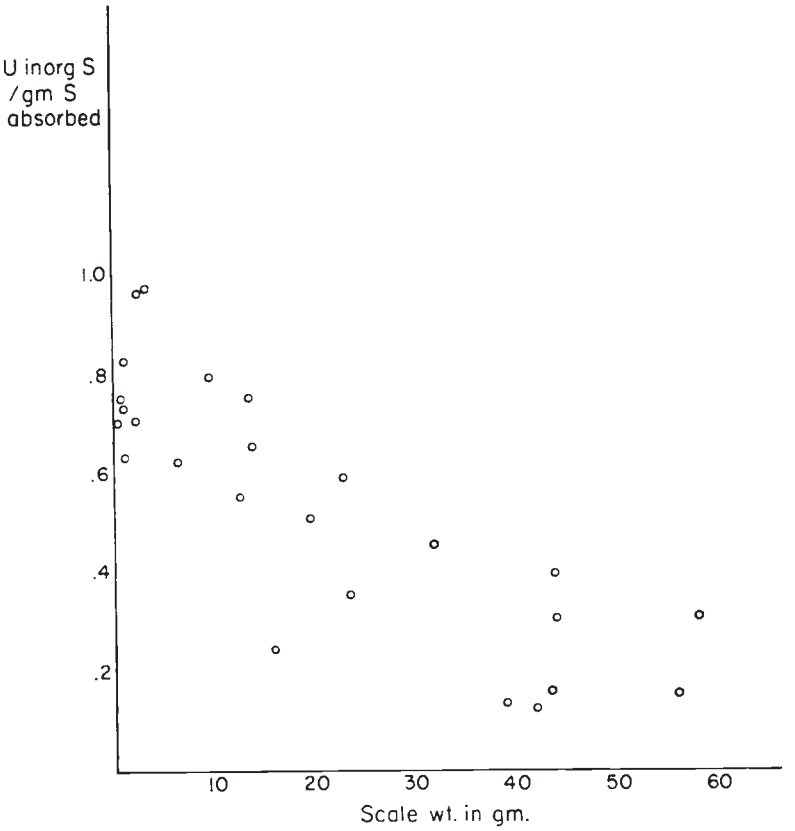

FIG. 2. Scattergram showing relationship between scale loss and urinary inorganic sulfate output per metabolic period.

above, it increases or decreases with the amount of protein metabolized (16). The variability in the percentage of total sulfur excreted as inorganic and total sulfate (inorganic plus ester sulfate) in the present control group reflects differences in sulfur absorption and thus is related to the dietary protein utilization.

Sabry, et al. (17), have recently shown the statistical correlation between urinary inorganic sulfate and the intake of methionine plus cystine. It may be assumed that our data with relation to absorbed sulfur represent mainly sulfur derived from the amino acids methionine and cystine. A fraction of the absorbed sulfur includes dietary cysteine, taurine, organic and inorganic sulfates as well as other sulfur containing compounds. Endogenous fecal sulfur losses have not been investigated and the term absorption has been used only to indicate the difference between intake and fecal excretion.

Increased epidermopoiesis in psoriasis is an anabolic process. Positive sulfur balance in the generalized form of this disease may be compared to positive sulfur balance previously demonstrated in growing children (18). Decreased urinary excretion of inorganic sulfate has also been reported in patients with advanced neoplastic diseases. This may be due to a decrease in the rate of intracellular oxidation of the sulfur containing amino acids which may be secondary to the sulfur requirements of the malignant tumor (19). It is still not clear whether the decreases in urinary inorganic sulfate excretion with increasing cutaneous losses in psoriasis represent in part, a peculiar response to this anabolic process or whether this is a non-specific homeostatic mechanism to compensate for nutrient losses from the skin. In order to prove or dis-

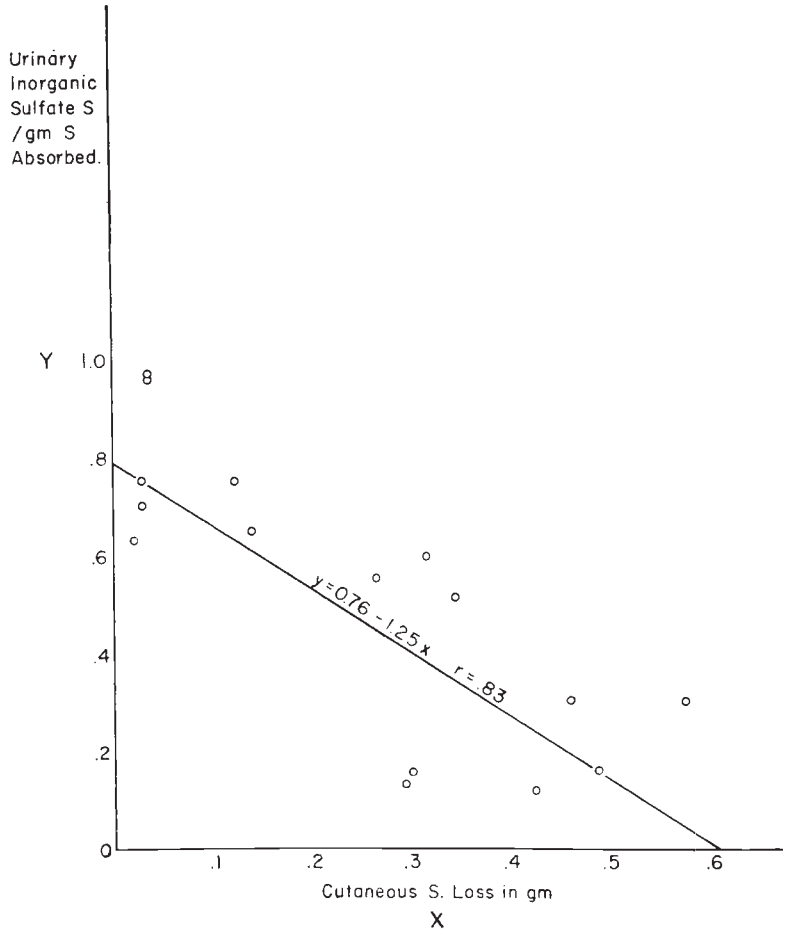

FIG. 3. Response of urinary sulfate excretion to increasing cutaneous loss per metabolic period.

TABLE IV

Metabolic response to exfoliation in case P.B. (female)

(Relationship between increased cutaneous and decreased urinary sulfur losses. Values in gm/6-day metabolic period.)

Metabolic period	Cumulative cutaneous sulfur loss	Urinary sulfur total	Excretion inorganic
1	0.206	1.780	0.795
2	0.782	2.037	0.833
3	1.244	2.030	0.795
4	1.732	1.506	0.429
5	2.026	1.109	0.369
6	2.330	1.023	0.404
7	2.752	0.935	0.399

prove the latter hypothesis, it will be necessary not only to study the metabolic response to exfoliation in other exfoliative dermatoses but also to demonstrate whether with increasing cutaneous losses there is reduced oxidation of sulfur containing amino acids, including methionine and cystine, derived from dietary protein.

SUMMARY

An investigation has been carried out to discover whether a homeostatic mechanism exists for the compensation of increased cutaneous nutrient losses. A group of psoriatic patients was studied in comparison with a group of control subjects. Complete sulfur balance studies were carried out in the two

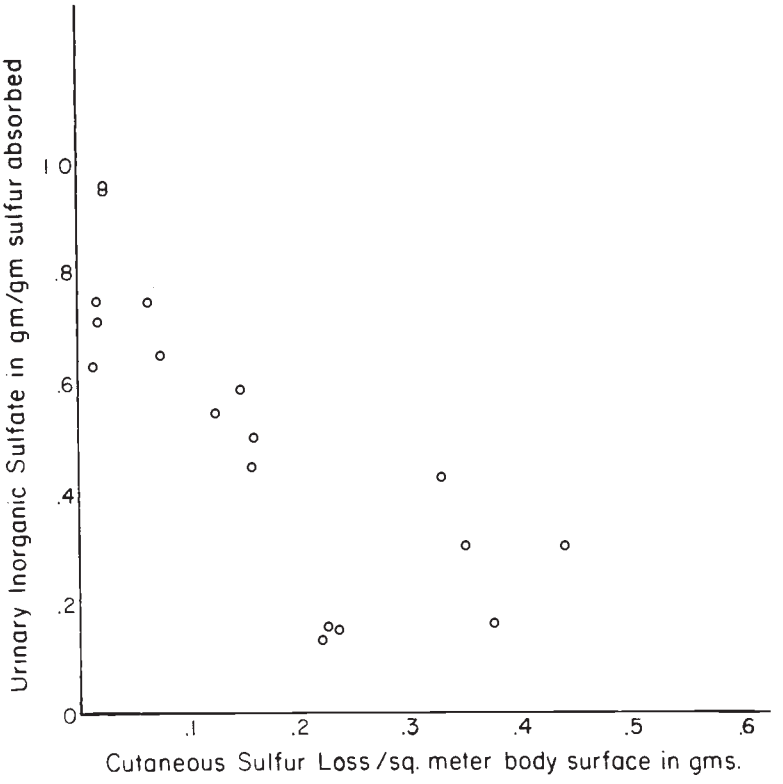

FIG. 4. Scattergram relating inorganic sulfate output in urine to corrected cutaneous losses per metabolic period.

groups including estimation of cutaneous losses and determination of the urinary partition of sulfur. It was shown that in the control group the absorption of sulfur was correlated with the urinary inorganic sulfate excretion, but that divergence from the relationship was found in the psoriatic group. In these subjects the urinary inorganic sulfate excretion was below that predicted by the regression line of sulfate excretion on sulfur absorption for the controls. An inverse relationship was found between the magnitude of the cutaneous losses and the cutaneous sulfur losses and the urinary inorganic sulfate excretion measured per gram of sulfur absorbed. The potential significance of these findings has been discussed with special reference to the implications of diminished sulfate excretion in persons with extensive dermatoses.

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